REMARKS

Claims 1-3, 5-6 and 14-17 are pending. Claims 4, 7-13, and 18-34 have been canceled. Claim 1 was amended to more clearly claim what Applicants consider to be their invention.

Claim 1 was amended to recite "and wherein the polypeptide is also capable of binding lipoproteins". Support for claim 1 can be found at least on page 55, lines 5-6 where binding of the claimed polypeptides to a lipoprotein is described.

Claim 3 was amended to recite "at least" 14 amino acids to 18 amino acids in length. Support for claim 3 can be found at least on page 17, lines 2-4 where polypeptides comprising 14 amino acids in length or about 18 amino acids in length.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

1. Claims 1 and 3 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

The Office Action alleges on page 2, lines 19-20 that it is unclear what the term "capable of" means. Applicants first note that claim 1 has been amended to further recite "and wherein the polypeptide is also capable of binding lipoproteins" thus reciting a functional element of the claim. As such, the claim now recites a specific sequence (i.e. SEQ ID NO: 210), a specific structure (i.e. capability of forming an amphipathic α helical structure), and a specific function (i.e. capability of binding lipoproteins). Applicants also note that the specification is replete with examples and descriptions of polypeptides that fall within the scope of claim 1 and a means for determining such. For example, the specification provides the sequence of SEQ ID. NO. 210 as

well as examples located within Tables 1-8 providing examples of polypeptides that have the claimed sequence. The specification also provides means to determine if the polypeptides that have the claimed sequence are capable of forming an amphipathic α helical structure (see page 45, line 26 – page 46, line 2 describing various computer programs that can be used to make such a determination). In addition, the Examples provide the means to determine whether a polypeptide can bind lipoproteins (see Examples 1-5, specifically Example 5).

The Office Action additionally appears to take issue with the use of the term "capable of" based on a notion that the claim might include proteins which do not themselves for amphipathic α helices, but after further modification or binding with some other molecule are incorporated into the helices. In response, Applicants submit that the claims specifically require the claimed polypeptides to have the recited structure, namely an amphipathic α helical structure. In other words, the claims do not encompass and "modified" peptides beyond peptides that have the recited structure. Therefore, the alleged alternate meaning of "capable of" does not and cannot apply to the claims

As such, Applicants submit that it would be clear, based on the description in the specification as well as the elements of the claim, to determine the scope of claim 1. Therefore, Applicants submit that the scope of claim 1 is therefore clear and complies with the requirements of 35 U.S.C. § 112, second paragraph.

Claim 3 was rejected for allegedly being unclear. Specifically, the Office Action alleges that the length of the polypeptides encompassed by claim 3 is unclear. Claim 3 was amended to recite "at least" 14 amino acids to 18 amino acids in length. Applicants submit that this is sufficient to overcome the rejection, and therefore respectfully request its withdrawal.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

1. Claims 1-3, 6, and 14-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Examiner alleges that the specification discloses several proteins within the scope of claim 1, but does not describe the full breadth of the genus claimed, i.e. that the use of "comprising" allows for additional amino acid residues to be added at either end of the peptide and the specification fails to describe which residues should be added or avoided to maintain an amphipathic α helical structure.

Applicants have provided a clear written description of what is required to fulfill the scope of the claims. Such a composition has been described in the specification. Section 2163 II.A.3 of the MPEP provides that possession can be shown by detailed disclosure of relevant identifying characteristics. Specifically, the MPEP provides:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Enzo Biochem*, 323 F.3d at 964, 63 USPQ2d at 1613...

MPEP 2163 II.A.3 (emphasis added).

Written description support for claim 1 is present throughout the specification where various non-limiting examples of peptides are described. For example, relevant identifying characteristics which provide evidence that Applicants were in possession of the claimed invention include the complete or partial structure of the peptide: the consensus sequence peptide (SEQ ID NO:210) and peptides truncated at the N-terminal or C-terminal ends (as provided in

Table 7). Relevant identifying characteristics also found throughout the specification include the following physical/chemical properties: non-limiting examples of peptides which have an increased angle subtended by its helix (see Table 1), DiMet-lysine analogs (see Table 2), peptides with varying ratios of arginine to lysine (see Tables 4 and 8), peptides with aromatic amino acids substituted with hydrophobic amino acids (see Table 5), and peptides with enhanced helicity (see Table 6). In addition, Table 9 lists non-limiting exemplary conservative amino acid substitutions for various amino acids and the specification teaches the skilled artisan how to select less conservative substitutions to change peptide function or immunological identity (for example, see the specification at pages 28-29).

The Examiner's insistence that the specification must list what additional residues are to be added to either the N- or C- terminus of the claimed peptide in order to describe the full breadth of the genus of polypeptides claimed (See Office Action, page 3, paragraph 4) has no basis in law. The MPEP specifically states:

> For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. As explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure."...An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) ....
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> What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies*, Inc., 802 F.2d at 1384, 231 USPQ at 94; See also *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005)("The 'written description' requirement must

> be applied in the context of the particular invention and the state of the knowledge.... As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution."). If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in ipsis verbis [i.e., "in the same words"] to be sufficient").

MPEP 2163 II.A.3 (emphasis added).

The Examiner further states on page 3 of the Office Action that the specification fails to describe which residues are to be added and which are to be avoided as the claim encompasses polypeptides larger than the recited 14-mer such that an amphipathic alpha helix is maintained. This is simply incorrect and untrue. Table 7 relates conservative substitutions that would maintain an amphipathic α helical domain. Furthermore, Example 1 teaches the skilled artisan that molecular modeling was performed to determine the helical structure of the single domain peptide of the invention given changes to the residues internal to the helix. The specification further teaches that molecular modeling programs such as WHEEL, LOCATE and HELNET described in a Journal of Lipid Research article can be used to identify and classify amphipathic α helical domains. Accordingly, the skilled artisan, with the instant specification in hand, would know which amino acid substitutions would maintain an amphipathic α helical structure and would also know to use programs such as WHEEL, LOCATE and HELNET to determine which residues are to be added and which are to be avoided such that a particular amino acid sequence could form an amphipathic α helical domain.

In addition, Applicants assert that compliance with the written description requirement need not involve the specific disclosure of every permutation of an invention, but should be commensurate with knowledge that comprises the state of the art. For example, in *Capon v.*

Eshhar v. Dudas 76 USPQ2d 1078, 1082 (Fed. Cir. 2005), the court remanded the case following appeal to the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences, where the board had previously decided that the specification of patents of both parties regarding production of chimeric genes designed to enhance immune responses failed to meet the written description requirement, thereby dissolving the interference and canceling the claims. The Board decided that it could not be known whether all the permutations and combinations covered by the claims would be effective for the intended purpose, and that the claims were too broad because they might include inoperative species. Specifically, the Board stated that the disclosure of specific examples provided in each party's specification, in the absence of any sequence information within the specification, did not provide adequate written descriptive support for the invention. In contrast, the court of appeals decided that since both parties presented specific examples of the production of specified chimeric genes, it was not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect was sufficiently demonstrated to characterize the invention.

The Court also confirmed its long-standing precedent that the disclosure required to meet the written description requirement will vary with the nature and scope of the invention. In sum, the Court concluded that knowledge, in the art, of the sequences of the nucleic acids that were joined to construct the chimeric DNA molecules, together with Appellants' disclosures of known methods for joining nucleic acid molecules to form chimeric DNAs, provided adequate written description of DNA molecules encoding chimeric receptors, and therefore recitation of exact nucleotide sequences was not required. Applicants assert that this same logic applies to the claimed synthetic apolipoprotein-E mimicking polypeptides

As provided above, Applicants have described the general structure, the component parts of the polypeptides, the physical/chemical properties; the secondary structure, as well as the operation of the claimed polypeptides. Applicants have also provided a number of examples of the claimed polypeptides. Like *Capon*, Applicants have provided specific examples of the claimed polypeptides, as well as clear guidance of how to select the components thereof, such as various substitutions. As stated by the court in *Capon*, it is not necessary that every permutation be effective in order for an inventor to obtain a generic claim, provided that the effect was sufficiently demonstrated to characterize the invention. Applicants submit that the claimed polypeptides were well demonstrated in the specification, as evidenced by the lengthy discussion of the claimed polypeptides provided throughout the specification and in the disclosed Table (see Tables 1, 2, 6, 7 and 9, as well as Example 1 for example).

Therefore, Applicants submit that the written description requirement is met, in that the applicant has clearly shown possession of the claimed polypeptides. For at least the reasons above, the present rejections should be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

1. Claims 1-3, 6, and 16-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Any analysis of whether a particular claim is enabled by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The test of enablement is whether one skilled in the art could make or

use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343, 199 USPQ 659 (CCPA 1976). A patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987). Determining enablement is a question of law based on underlying factual findings. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984).

The Office Action on page 3, lines 17-18, alleges that claims 1-3, 6, and 16-17 do not provide enablement for the broad genus of polypeptides as claimed in pending claim 1. The rejection relies on the notion that because the sequence provided in claim 1 is broader than claims 5, 14 and 15 that it would require undue experimentation to determine how to use the claimed polypeptides commensurate with the scope of claim 1.

First, Applicants note that claim 1, from which claims 2-3, 6, and 16-17 depend, has been amended to recite and wherein the polypeptide is also capable of binding lipoproteins. Applicants would also like to point out that MPEP (Section 2164.02) states that, "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation."

Here, the specification provides full representative examples of the claimed genus of polypeptides and their capability of binding lipoproteins. For example, Example 5 of the instant specification shows that the claimed polypeptides bind to lipoproteins. Example 5 also shows that the claimed polypeptides can reduce serum cholesterol, in part by reducing VLDL and IDL/LDL fractions. Examples 1-4 also reveal methods of reducing serum cholesterol using the claimed polypeptides that involves binding and removing various lipoproteins from cells. The Examiner has not advanced adequate reasons for why a person skilled in the art could not use the genus as claimed as a whole without undue experimentation. Accordingly, the disclosure provided in the Examples would enable one of skill in the art to make and use the claimed invention without undue experimentation.

Furthermore, as provided above a patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987). As specified on page 3, lines 11-12, it is well known in the art that Apolipoprotein E is a protein that binds lipids (Mahley, R.W., et al. *J. Lipid Res.* 1999, 40:622-630). Here, the claimed peptides are synthetic apolipoprotein-E mimicking polypeptides that, in part, are capable of binding lipoproteins. The specification goes on to support such a function on page 55, lines 5-6 where the binding of the claimed polypeptides to a lipoprotein are described. Applicants again submit that one of skill in the art could make or use the claimed invention from the disclosures in the patent (e.g. the Examples) coupled with information known in the art (e.g. Mahley et al.) without undue experimentation.

For all of the above reasons, Applicants submit that the present claims are fully enabled. As such, Applicants respectfully request withdrawal of this rejection.

A Credit Card payment in the amount of $60.00, representing the fee pursuant to 37 C.F.R. §1.17(a)(1) and a Request for Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

Scott D. Marty
Registration No. 53,277

NEEDLE & ROSENBERG, P.C.
Customer Number 23859
(678) 420-9300
(678) 420-9301 (fax)

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Scott D. Marty, Ph.D.

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